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Knobbe Martens Olson & Bear LLP
2040 Main Street
Fourteenth Floor
Irvine, CA 92614

EXAMINER

Forman, Betty J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/782,588	Applicant(s) KAIN ET AL.	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-12, 18-25 and 27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 6-12 18-25 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 6 August 2003 in which a response to the Office Action of 6 February 2003 was submitted. It is noted that the listing of claims provided in the response incorrectly numbers Claim 27 as Claim 26.

The previous rejections as reiterated below are maintained. The previous rejections over Fan et al are withdrawn in view of Applicant's comments.

All of the arguments have been thoroughly reviewed and are discussed below.

Claims 1-4, 6-12, 18-25 and 27 are under prosecution.

Priority

2. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, Provisional Application 60/181,631 filed 2 February 2000 upon which priority is claimed does not provide adequate support under 35 U.S.C. 112 for claims 1-4, 6-12 and 18-25 of this application. Specifically, the '631 application does not teach or describe random distribution of microspheres on a substrate surface; does not teach or describe a distance between centers of a first and second microsphere of a subpopulation; and does not teach or describe a **ratio** of first and second subpopulations. Because the '631 application does not teach or describe the above limitations recited in the instant claims, the '631 application does not provide adequate support under 35 U.S.C. 112, for the instant claims. Therefore, the

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effective filing date for the instant claims is the filing date of the instant application i.e. 12 February 2001.

Response to Applicant's Comments

3. Applicant argues that page 2, ¶ 5 the '631 application discloses a first and second subpopulation. The examiner has reviewed page 2 and acknowledges the disclosure of first and second subpopulations. However, as noted above, the '631 application does not teach a ratio of first and second subpopulations.

Applicant argues that support for the limitation "random distribution of microspheres on a substrate surface is provided on page 1, number 4, second and third paragraphs of the '631 application. The cited passage recites "randomly assembled Bead Arrays™ and Array of Arrays™". Applicant asserts that "randomly assembled array, in the context of this application, necessarily means that the microspheres are randomly distributed on the surface of the substrate because the arrays are bead based and assembly requires distribution of the beads on the surface of the substrate." The argument has been considered but is not found persuasive because in the recitation "randomly assembled arrays", "randomly" describes the assembly of the arrays but the recitation does not limit or require that the **beads** of the arrays are randomly distributed on a surface as instantly claimed. As such, the cited passage does not provide support for the instantly claimed random distribution of microspheres on a substrate surface.

Applicant states that the '631 (at the bottom of page 1) provides support to the instantly claimed distance between centers of first and second microspheres of at least 5µ m. The cited passage describes bead **spacing** of from <15µ m to 15-20µ m. The cited passage does not teach or describe a **distance between centers** as instantly claimed. The instantly claimed "distance between the centers" describes a measurement between the center of one bead to the center of another bead. As such, a teaching of bead spacing does not describe a distance between centers as instantly claimed.

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As such, the '631 application does not provide support of the instant claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-4, 6-7, 9-12, 18-20 and 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Brenner (U.S. Patent No. 5,863,722, issued 26 January 1999).

Regarding Claim 1, Brenner discloses a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50µm (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 50µm (Column 10, lines 30-35 and Column 20, lines 32-35); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface

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(Column 20, lines 42-46) wherein the substrate comprise the dimensions of a microscope slide (Column 19, lines 55-60 and Fig. 5).

Regarding Claim 2, Brenner discloses the composition wherein the sites are separated by a distance of less than $25\text{ }\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than $25\text{ }\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 3, Brenner discloses the composition wherein the sites are separated by a distance of less than $15\text{ }\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than $15\text{ }\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 4, Brenner discloses the composition wherein the sites are separated by a distance of at least about $5\text{ }\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about $5\text{ }\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 6, Brenner discloses the composition wherein the distance between centers of a first and second subpopulations is at least $5\text{ }\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about $5\text{ }\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 7, Brenner discloses the composition wherein the distance between a first and second microspheres is less than $100\text{ }\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than $100\text{ }\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 9, Brenner discloses the composition wherein the distance between a first and second microspheres is less than $100\text{ }\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than $100\text{ }\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

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Regarding Claim 10, Brenner discloses the composition wherein the distance between a first and second microspheres is less than $50\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than $50\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 11, Brenner discloses the composition wherein the distance between a first and second microspheres is less than $15\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than $15\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 12, Brenner discloses the composition wherein the sites are separated by a distance of at least about $5\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about $5\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 18, Brenner discloses a method for making a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than $50\mu\text{m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than $50\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (Column 20, lines 42-46) wherein the substrate comprise the dimensions of a microscope slide (Column 19, lines 55-60 and Fig. 5).

Regarding Claim 19, Brenner discloses the method wherein the sites are separated by a distance of less than $25\mu\text{ m}$ (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than $25\mu\text{ m}$ (Column 10, lines 30-35 and Column 20, lines 32-35).

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Regarding Claim 20, Brenner discloses the method wherein the sites are separated by a distance of less than 15 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 15 μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 23, Brenner discloses the composition wherein the distance between centers of a first and second subpopulations is at least 5 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about 5 μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 24, Brenner discloses the composition wherein the distance between centers of a first and second subpopulations is at least 15 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about 15 μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 25, Brenner discloses the method wherein the distance between a first and second microsphere is at least 50 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 50 μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Response to Arguments

6. Applicant argues that Brenner does not teach discrete sites separated by a distance of less than 50 μ m. The argument has been considered but is not found persuasive because as cited above, Brenner clearly teaches the discrete site are separated by a distance equal to a diameter of the microparticle (Column 20, lines 30-35) and Brenner teaches microparticle diameter of 1-2 μ m (Column 10, lines 30-33). Therefore, Brenner teaches separation of the sites by less than 50 μ m as claimed.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-4, 6-12, 18-20 and 23-25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 98/40726, published 17 September 1998) in view of Noonan et al (U.S. Patent No. 6,129,896, filed 17 December 1998) and Van Ness et al (U.S. Patent No. 6,248,521, issued 19 June 2001).

Regarding Claim 1, Walt et al teach a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50 μ (Fig. 5); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (page 17, line 13-page 18, line 24). Walt et al teach that the substrate comprises a plurality of fibers arranged into a bundle for optimal observation via their microscope objective lens (page 19, lines 15-25) but they do not teach their substrate comprises the dimensions of a microscope slide. However, it was well known in the art at the time the claimed invention was made that fiber optic bundles can be formatted to desired dimensions as taught by Noonan et al. (Abstract) and Van Ness et al teach a motivation for formatting the substrate to have the dimensions of a microscope slide i.e. a substrate having the dimensions of a glass slide is easily illuminated and detected using a microscope (Column 10, lines 27-41). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Walt et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious

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benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 10, lines 27-41).

The courts have stated that claimed dimensions of a known device do not distinguish over the prior art device when the claimed device would not perform differently from the prior art device. *In Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

The courts have stated that absent evidence to the contrary, a particular configuration of a known device is a matter of choice which would have been obvious to one skilled in the art. *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966) (The court held that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.).

Regarding Claim 2, Walt et al teach the composition wherein the sites are separated by a distance of less than 25 μ m (Fig. 5).

Regarding Claim 3, Walt et al teach the composition wherein the sites are separated by a distance of less than 15 μ m (Fig. 5).

Regarding Claim 4, Walt et al teach the composition wherein said sites are separated by a distance of less than 15 μ m (Fig. 5) but they do not teach the separation is at least 5 μ m. However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation distance of Walt et al using routine experimentation to thereby derive an optimal separation distance (e.g. at least 5 μ m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

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It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 6, Walt et al teach the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 5 μ m (Fig. 5).

Regarding Claim 7, Walt et al teach the composition wherein the distance between a first and second microspheres is less than 100 μ m (Fig.5).

Regarding Claim 8, Walt et al teach the composition wherein the substrate further comprises first and second assay locations (i.e. wells) and wherein said first and second subpopulations are distributed in said assay locations (page 22, lines 8-30).

Regarding Claim 9, Walt et al teach the composition wherein the distance between a first and second microsphere is less than 100 μ m (Fig. 5).

Regarding Claim 10, Walt et al teach the composition wherein the distance between a first and second microsphere is less than 50 μ m (Fig. 5).

Regarding Claim 11, Walt et al teach the composition wherein the distance between a first and second microsphere is less than 15 μ m (Fig. 5).

Regarding Claim 12, Walt et al teach the composition wherein the distance between centers of a first and second subpopulations is at least 2.2m m (Fig. 5) but they do not specifically teach the distance between the microspheres is at least 5 μ m. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Walt et al using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5 μ m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

Regarding Claim 18, Walt et al teach a method for making a composition comprising: providing a substrate with a surface comprising discrete sites said sites separated by a

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distance of less than 50 μ m (Fig. 5); and randomly distributing a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive (page 17, line 13-page 18, line 24). Walt et al teach that the substrate comprises a plurality of fibers arranged into a bundle for optimal observation via their microscope objective lens (page 19, lines 15-25) but they do not teach their substrate comprises the dimensions of a microscope slide. However, it was well known in the art at the time the claimed invention was made that fiber optic bundles can be formatted to desired dimensions as taught by Noonan et al. (Abstract) and Van Ness et al teach a motivation for formatting the substrate to have the dimensions of a microscope slide i.e. a substrate having the dimensions of a glass slide is easily illuminated and detected using a microscope (Column 19, lines 27-41). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Walt et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 19, lines 27-30).

The courts have stated that claimed dimensions of a known device do not distinguish over the prior art device when the claimed device would not perform differently from the prior art device. *In Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

The courts have stated that absent evidence to the contrary, a particular configuration of a known device is a matter of choice which would have been obvious to one skilled in the art. *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966) (The court held that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.).

Regarding Claim 19, Walt et al teach the method wherein said wells are separated by distance of less than $25\mu\text{ m}$ (Fig. 5).

Regarding Claim 20, Walt et al teach the method wherein said wells are separated by distance of less than $15\mu\text{ m}$ (Fig. 5).

Regarding Claim 23, Walt et al teach the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least $5\mu\text{ m}$ (Fig. 5).

Regarding Claim 24, Walt et al teach the method wherein the distance between centers of a first and second subpopulations is at least $5\mu\text{ m}$ (Fig. 5) but they do not specifically teach the distance between centers is at least $15\mu\text{ m}$. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Walt et using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5 m and at least 15 m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 25, Walt et al teach the method wherein the distance between microspheres is at least $5\mu\text{ m}$ (Fig. 5) but they do not specifically teach the distance between microspheres is at least 50 m . It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between microspheres on the substrate of Walt using routine experimentation to thereby derive an optimal distance (e.g. at least 50 m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

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It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 27, Walt et al teach the method wherein the discrete sites are wells (page 7, lines 5-9).

Response to Arguments

9. a. Applicant argues that the cited prior art does not provide the required motivation or suggestion to combine their teachings. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

b. In this case, Walt et al teach that the substrate comprises a plurality of fibers arranged into a bundle for optimal observation via their microscope objective lens (page 19, lines 15-25) which clearly suggests that the substrate has the dimensions of a microscope slide. Furthermore, it was well known in the art that fiber optic bundles can be formatted to desired dimensions (i.e. predetermined arrangement) as taught by Noonan et al. (Abstract) and Van Ness et al teach a motivation for formatting the substrate to have the dimensions of a microscope slide i.e. a substrate having the dimensions of a glass slide is easily illuminated and detected using a microscope (Column 19, lines 27-41). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Walt et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious

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benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 19, lines 27-30).

c. Applicant argues that Noonan et al, in the cited Abstract, does not teach individual fibers can be formatted to desired dimensions. The argument has been considered but is not found persuasive because Noonan et al clearly teach a “predetermined arrangement” of the fibers whereby the desired substrate is created (Abstract) and further define “predetermined arrangement (e.g. circle, square etc., Column 2, line 64-Column 3, line 30). Therefore, it would have been obvious to one of ordinary skill in the art that the substrate can be formatted as desired (e.g. circle, square) based on the teachings of Noonan et al.

d. Applicant argues that VanNess teaches away from the instantly claimed random distribution of microspheres. The argument has been considered but is not found persuasive because Walt et al teaches random distribution of microspheres (page 17, line 13-page 18, line 24). Van Ness provides a motivation for formatting a substrate to have the dimensions of a microscope slide i.e. a substrate having the dimensions of a glass slide is easily illuminated and detected using a microscope (Column 19, lines 27-41). The fact that Van Ness does not teach all limitations of the claims e.g. random distribution, does not negate the fact that Van Ness provides motivation for providing substrates having glass slide dimensions.

e. Applicant argues that the Office has applied an “obvious to try” standard in making the above rejection because the cited references do not teach or suggest their combination. The argument has been considered but is not found persuasive because as discussed above in sub-paragraph “b”, the references provide suggestion and motivation.

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10. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 998/40726, published 17 September 1998) in view of Noonan et al (U.S. Patent No. 6,129,896, filed 17 December 1998) and Van Ness et al (U.S. Patent No. 6,248,521, issued 19 June 2001) as applied to Claim 18 above and further in view of Gentalen et al (U.S. Patent No. 6,306,643 B1, filed 24 August 1998).

Regarding Claims 21 and 22, Walt et al is silent regarding a ratio between microsphere subpopulations. However, ratios of subpopulations were well known in the art at the time the claimed invention was made as taught by Gentalen et al who teach that subpopulation ratios are derived based on experimental design (Column 11, lines 13-44 and Claim 9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the ratio of first and second subpopulations based on experimental design to thereby optimize experimental results. For example, for an experiment designed to detect nucleic acid sequences expressed in low copy number, the skilled practitioner in the art would have been motivated to provide subpopulations of nucleic acid microspheres in a ratio of 1:36 or 1:100 (high copy number sequence:low copy number sequence) to thereby detect the low copy number sequence without signal interference from the high copy number sequence. In this experimental design it would have been obvious to one of ordinary skill in the art to modify the low copy to high copy number ratio using routine experimentation to thereby optimize experimental conditions and to maximize detection of low copy number.

Response to Arguments

11. Applicant argues that Gentalen et al do not cure the deficiencies of Walt, Van Ness and Noonan and therefore the rejection is improper. The argument has been considered but is not found persuasive for the reasons stated above regarding Walt, Van Ness and Noonan.

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12. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner (U.S. Patent No. 5,863,722, issued 26 January 1999) in view of Gentalen et al (U.S. Patent No. 6,306,643 B1, filed 24 August 1998).

Regarding Claims 21 and 22, Brenner teaches the method for making a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 50 μ m (Column 10, lines 30-35 and Column 20, lines 32-35); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (Column 20, lines 42-46) wherein the substrate comprise the dimensions of a microscope slide (Column 19, lines 55-60 and Fig. 5). Brenner is silent regarding a ratio between microsphere subpopulations. However, ratios of subpopulations were well known in the art at the time the claimed invention was made as taught by Gentalen et al who teach that subpopulation ratios are derived based on experimental design (Column 11, lines 13-44 and Claim 9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the ratio of first and second subpopulations based on experimental design to thereby optimize experimental results. For example, for an experiment designed to detect nucleic acid sequences expressed in low copy number, the skilled practitioner in the art would have been motivated to provide subpopulations of nucleic acid microspheres in a ratio of 1:36 or 1:100 (high copy number sequence:low copy number sequence) to thereby detect the low copy number sequence without signal interference from the high copy number sequence. In this experimental design it would have been obvious to one of ordinary skill in the art to modify the low copy to high copy number ratio using routine experimentation to thereby optimize experimental conditions and to maximize detection of low copy number.

Response to Arguments

13. Applicant argues that Gentalen et al do not cure the deficiencies of Brenner and therefore the rejection is improper. The argument has been considered but is not found persuasive for the reasons stated above regarding Brenner.

14. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



BJ Forman, Ph.D.
Primary Examiner
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October 29, 2003